Understanding the status of the X chromosomes in human ESCs and preimplantation embryos

Grant Award Details

Understanding the status of the X chromosomes in human ESCs and preimplantation embryos

Grant Type: Basic Biology IV

Grant Number: RB4-06133

Project Objective: The overall goal is to gain insight into the mechanisms that lead to the acquisition of X chromosome states in hESC, to understand the consequences of various X states on cell fate, and to develop methods to control X states.

Investigator:

Name:	Kathrin Plath
Institution:	University of California, Los Angeles
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Cell Line Generation: Embryonic Stem Cell

Award Value: $1,382,400

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Understanding the status of the X chromosomes in human ESCs and preimplantation embryos

Public Abstract: Human embryonic stem cells (hESCs) are able to divide indefinitely and under the proper conditions, can essentially become any cell in the human body. They are derived from the developing human embryo and carry great promise for regenerative medicine. However, these cells demonstrate an instability surrounding the state of the X chromosome. Male (XY) cells and female (XX) cells use a mechanism called X chromosome inactivation (XCI) to achieve equal expression of genes on the X chromosomes. XCI happens specifically in female cells and shuts down one of the two X chromosomes. The silencing of the X chromosome is a life-or-death decision that is made early in development, but when exactly remains unclear. Female cells from humans always possess one inactive and one active X chromosome. hESCs with the same X inactivation pattern as adult cells and those that have not undergone XCI have been derived, yet the cause for this heterogeneity is unknown. Given that lines can change their XCI state over time, and this volatility may have far-reaching impact, we propose to study why this happens. In addition, we will test whether the different X chromosome states affect the utility of hESCs.

Statement of Benefit to California: The proposed project will benefit the state of California and its citizens as follows:

1. Human embryonic stem cells could revolutionize modern medicine if used in cell-based therapies. However, the translational use of hESCs will not be realized unless we can ensure reproducible derivation of high quality stem cells. Our proposal works towards identifying markers that can be used as benchmarks to assess the quality of female hESCs. Therefore, our work will have practical implications for stem cell therapy and the use of hESCs in disease studies and basic biology.

2. Our team is composed of two research groups with expertise in stem cell biology. In addition to creating highly skilled jobs, the proposed research activities will create an interdisciplinary education environment for training the next generation of California citizens at all levels, including high school, undergraduate, graduate students, as well as postdoctoral fellows.

3. All scientific findings produced from these studies will be publicly available to non-profit and academic organizations in California, and any intellectual property developed by this project will be developed under the guidelines of CIRM to benefit the State of California.

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